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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,658	06/30/2003	Richard A. Thomas	P-RT 3600A	1988

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EXAMINER

SKIBINSKY, ANNA

ART UNIT PAPER NUMBER

1631

DATE MAILED: 09/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/611,658

Applicant(s)

THOMAS, RICHARD A.

Examiner

Anna Skibinsky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-66 is/are pending in the application.
- 4a) Of the above claim(s) 1-30, 39-42, 47, 48, 51-53, 59, 60 and 62-66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-38, 43-46, 49, 50, 54-58 and 61 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 5 pages. 9/2/2003
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claim Election/Restriction

1. Applicant's election without traverse of Group II, Species F9, G1, H1, I1, and J1 corresponding to claims 31-38, 43-46, 49, 50, 54-58, and 61 in the reply filed on June 16, 2006, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 1-30, 39-42, 47, 48, 51-53, 59, 60, 62-66 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group and Species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on June 16, 2007.

Claim Rejections - 35 USC § 101

Claims 31-38, 43-46, 49, 50, 54-58, and 61 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Said claims contain a non-statutory embodiment wherein the method of determining a nuclear packing efficiency as claimed can be carried out on a computer involving the manipulation of data without a concrete, tangible, and useful result. Though the properties calculated by the model are physical properties, the data is nonetheless generated within a computer without a physical manifestation. For example, the measuring of biochemical component (BC) and spatial displacement of the nucleus

recited in steps (a)(1) and (a)(2) can be done from data residing in the memory of a computer and not directly from a physical sample. Thus, the claims currently have a non-statutory embodiment which does not meet the standard of being concrete, tangible and useful.

The claims "must be for a practical application of the abstract idea, law of nature, or natural phenomenon. Diehr, 450 U.S. at 187, 209 USPQ at 8 ("application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection."); Benson, 409 U.S. at 71, 175 USPQ at 676 (rejecting formula claim because it "has no substantial practical application").

To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways:

1) The claimed invention "transforms" an article or physical object to a different state or thing.

2) The claimed invention otherwise produces a useful, concrete and tangible result, based on the factors discussed in MPEP 2106, and See also:

http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/guidelines101_20051026.pdf

The manipulation of coordinates and interaction energies or residues to calculate the crossover point is the manipulation of numbers, performed by the computer implementing programs and is therefore nonstatutory subject matter. Manipulation of data does not include a physical transformation outside of a computer or representation thereof. A process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter

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and is not deemed to be concrete, tangible, and useful and is therefore non-statutory.

An example which would make the instant method steps statutory would be to include a step of displaying the data for a user. Hence, the result would become concrete, tangible, and useful.

Claim Rejections - 35 USC § 112-2nd paragraph

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 31-34, 37, 38, 43-46, 49, 50, 54-58, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 31 recites "NPE" without a definition. Abbreviations and acronyms are vague and indefinite in claims unless accompanied by the entire name to explain what is meant. Please correct by including the entire phrase corresponding to "NPE" Claims which are dependent from claim 31 also contain this unclarity due to their dependence. For the purpose of examination NPE is interpreted as nuclear packing efficiency.

Claim 46 recites "the geometric parameter is increased major axis" which is unclear. For the purpose of examination, this will be interpreted as the geometric parameter increases along the major axis.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claim 31-38, 43-46, 49, 50, and 54-58 are rejected under 35 U.S.C. 102(b) as being anticipated by Irinopoulou et al. (1998). Irinopoulou et al. has already been provided on applicant's IDS.
4. The instant claims recite a measuring a biochemical component (BC) and a special displacement of the nucleus (SDN) of the cell for a number of cells in a population, determining a data point for the BC and SDN (claim 31). The BC, as taught by the specification includes the DNA content (specification, page 10, lines 5-8), while the SDN is the volume occupied by the nucleus (specification, page 7, lines 16-18). A geometric parameter is then determined from the slope of a line that passes through the cluster of data points (claims 32, 33, and 34) and the origin of the axes. The nuclear packing efficiency (NPE) is then determined according to the preselected geometric parameter for the cluster of data points (claims 31 and 37) that are plotted on a axes with predefined range (claim 38).
5. Irinopoulou et al. teach image cytometry to measure the DNA content which is plotted on one axes of a graph against the nuclear volume of cell nuclei (page 351, col. 1, lines 1-3; and page 355, Figure 3 and col. 1, lines 17-19). The clusters of data points corresponding to the DNA content and nuclear volume are extrapolated with four

regression lines, each of which have a different slope and pass through the origin of the axes (page 355, Figure 3). The slopes are used to assess the cases of cells with hyperplasia, well and poorly differentiated carcinoma, and prostatic intraepithelial neoplasia (PIN) cells (page 354, col. 2, lines 21-24). The volume to DNA content correspondence is used to determine that the PIN case has a higher content of non-DNA molecules which also indicates how the nuclear packing in relation to how nuclei pack in the other cases where the cells with same DNA content have a smaller nuclear volume.

6. The instant claims further recite identifying the cell if the cell's NPE is within at least one predetermined NPE range (claim 35) and segregating the identified cell from the non-identified cells (claim 36).

7. Irinopoulou et al. show (page 355, Figure 3) how the PIN cells have a cluster, that when extrapolated has a line with a smaller slope than the slopes for the other clusters. The PIN slope stands out from the other three lines and is used to identify the PIN cell nuclei.

8. The instant claims further recite that the cells are in the S cycle (claims 44 and 45). The geometric parameter is increasing along the major axis for the plotted cells (claim 46). The cells are furthermore in a state of genetic disease (claims 49, 50 and 57) and wherein the cell phenotype is aneuploidy (claim 54) or neoplastic (claim 55). The geometric parameter is the reduced slope of the gradient line (claim 58).

9. Irinopoulou et al. teach the study of cells in the state of carcinoma and prostatic intraepithelial neoplasia (PIN) where the cells are also in diploid, triploid and tetraploid

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states indicating aneuploidy and the passing through cellular division and the S cycle. In Figure 3 (page 355), the major axis is the x-axis where volume is plotted, which shows a greater increase than the corresponding increase in DNA content. Thus, the geometric parameter which is the regression line shows a greater increase in values along the major axis. Furthermore, the gradient of the four regression lines shows a reduced slope for the line extrapolated through the NIP cluster.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 31-34, 37, 38, 43-46, 49, 50, 54-58, and 61 rejected under 35 U.S.C. 103(a) as being unpatentable over Irinopoulou et al. as applied to claims 31-34,

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37, 38, 43-46, 49, 50, and 54-58 above, and further in view of Baldetorp et al.

(Cytometry, 1992).

13. Irinopoulou et al. teaches the study of prostate tissue using image cytometry and plotting the DNA content of prostate cell nuclei vs. the volume of the nuclei.

Irinopolou however does not teach this method as applied to breast tissue, as required by claim 61.

14. Baldetorp et al. however teaches the study of breast cancer cells and DNA ploidy and aneuploidy that results using DNA image cytometry (Abstract).

15. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have applied the technique taught by Irinopoulou et al. to the study of breast nuclei in breast tissue. One of skill in the art would have been motivated to image cytometry as taught by both Irinopoulou et al. and Baldetorp et al. to study the DNA content to nuclei volume behavior as taught by Irinopoulou et al. (Irinopoulou et al., Figure 3) since the breast tissue of Baldetorp et al. is also aneuploid (Baldetorp et al., Abstract).

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

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obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

17. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

18. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 31-34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6 and 21-23 of U.S. Patent No. 6,587, 792. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 31-34 of the instant application are verbatim identical with claims 6 and 21-23 of U.S. Patent No. 6,587, 792, except that claim 6 of

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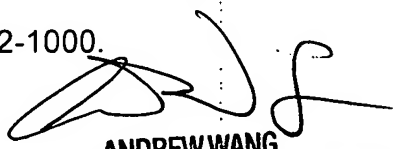
the Patent recites measuring the SDN of the cell "using nuclear envelope volume". The "using nuclear envelope volume" is not specifically defined in the cell and is interpreted as being the volume of the nucleus which is the meaning applied to SDN (specification, page 7, lines 16-18) as discussed above. Thus, both claims 31 of the instant application and 6 of the Patent describe the same invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anna Skibinsky whose telephone number is (571) 272-4373. The examiner can normally be reached on 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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